JUL 8 1930

AMERICAN JOURNAL *of* PHARMACY

SINCE 1825

A Record of the Progress of Pharmacy and the Allied Sciences

COMMITTEE ON PUBLICATION

Charles H. LaWall, Ph. M., Sc. D. — Joseph W. England, Ph. M. — J. W. Sturmer, Pharm. D.
John K. Thum, Ph. M. — Arno Viehoever, Ph. D. — E. Fullerton Cook, Ph. M.

Special Contributor, Henry Leffmann, A. M., M. D.

IVOR GRIFFITH, Ph. M., Editor

Vol. 102 — JUNE, 1930 — No. 6

CONTENTS

Editorial:
Malt Extracts 295

Original Articles:
The Chemist as a Detective. By Charles H. LaWall, Philadelphia, Pa. 297

Enteric Coatings. By Milton S. Wruble, Philadelphia, Pa. 318

Certified Food Colors: Their Characteristics and Tests. By M. C. Gallagher and L. E. Owen, Chicago, Ill. 329

Medical and Pharmaceutical Notes 338

News Items and Personal Notes 344

Book Review 347

Price $3.00 per Annum in Advance — Foreign Postage, 25 Cents Extra

Single Numbers, 30 Cents. Back Numbers, 50 Cents

Entered as Second-Class Matter at the Post Office at Philadelphia, Pa., Under the Act of March 3, 1879

Acceptance for Mailing at Special Rate of Postage Provided for in Section 1103, Act of October 3, 1917, Authorized February 15, 1920

PUBLISHED MONTHLY BY THE

Philadelphia College of Pharmacy and Science

43d Street and Kingsessing Avenue, West Philadelphia, Pa.

Have you noted how extensively PANTOPON 'ROCHE' is being prescribed *in place of morphine?* . .

The trend from morphine to PANTOPON is marked . . . . . .

Up-to-the-minute 1930 Prescription Pharmacies keep PANTOPON 'ROCHE' in stock . . . . . .

IN PLACE OF MORPHINE FOR PAIN AND SEDATION, ⅓ GR. PANTOPON IS PRESCRIBED WHERE ¼ MORPHINE WOULD USUALLY BE USED

IN PLACE OF CODEINE IN COUGH PRESCRIPTIONS ½ GR. PANTOPON IS USED TO THE DOSE . . . . . .

Powder: vials of 1, ½, ¼ and ⅛ oz. . . . . . *Ampuls: ⅓ gr. (1.1 cc.) cartons of 6 and 12.* . . . .

Hypodermic tablets: ⅓ gr., tubes of 20. . . . . . *Oral tablets: ⅙ gr. vials of 20.*

An interesting booklet "The Juice of the Poppy" will be sent to pharmacists, free of charge on request

Hoffmann-La Roche, Inc.

Makers of Medicines of Rare Quality

NUTLEY NEW JERSEY

THE AMERICAN
JOURNAL OF PHARMACY

VOL. 102 JUNE, 1930 No. 6

EDITORIAL

MALT EXTRACTS

THE PRESENCE OF AN ACTIVE starch-converting enzym in malt led to its extensive use in the treatment of real or supposed lack of active salivary or pancreatic digestion. Malt extracts were offered in two forms; liquid and semi-solid. Examinations of the familiar commercial forms were made by me many years ago, and reported through a local medical journal. All the liquid forms were found to contain alcohol and to be without diastatic power. The semi-solid non-alcoholic forms, known respectively as "Maltine" and "Trommer's Malt" had notable diastatic power, especially the former. In the course of the examination it was found that salicylic acid, then much used as a preservative for malt liquors, interfered with the action of diastase, notwithstanding which fact one of the liquid extracts contained it. The liquid extracts found considerable sale in consequence of the presence of alcohol, being used as a polite substitute for beer. Some of them contained more alcohol than the average lager.

In recent years many brands of malt extract and malt syrup have appeared on sale and are found in special stores and, in some parts of the country, in grocery stores. These are, however, mixed with a substance—hop extract—that was never found in the preparations offered before the advent of the prohibition amendment. The remarkable eruption of what is generally advertised as "malt extract, hop flavored," or somewhat similar phrase, has attracted the attention of the officials charged with the enforcement of the Volstead Act. A decision has recently been given by the United States Supreme Court that the sale of such products and accessory articles, such as bottles and caps, may constitute an intention to violate the provisions of that act and be, therefore, punishable under it. It appears, how-

ever, that the articles must be sold for the "purpose" of making "home brew," otherwise the sale is not in violation of any existing statute. The usual ingenuity of commercialism in such cases has been fully shown by the dealers in these articles. They are advertised for bread making and other real food purposes. In view of the opinion of the public at large concerning prohibition laws, it may be difficult to get conviction in most cases.

Meanwhile, a valuable series of analyses of the numerous hopped-malt extracts now offered has been made in the laboratory of the New Hampshire State Board of Health. The chief chemist, Mr. Charles D. Howard, has reported the results in detail in the May issue of the special bulletin (*Health*) of the board. Mr. Howard's investigation has been comprehensive and thorough. Forty-seven samples were examined as to total solids, mineral matter, acidity as lactic acid, diastatic power (U. S. P. test) and presence of non-malt sugars. Three samples showed the required diastatic power, several had slight power. Many contained other carbohydrates than maltose. The texts of the labels show the "base uses" to which language may be brought. All but three of the samples are stated to be "hop flavored." As almost all the labels declare that the article is intended for bread or candy making, it appears that the American public has suddenly become addicted to hop flavor in its "staff of life" and "sweets." Yet advertising experts tell us that in these days advertising is by long odds perfectly honest and straightforward!

There is no question, of course, that these articles are placed upon the market for making malt liquors. State and national authorities can at least prevent any claim of starch-digesting power upon which the dietetic and therapeutic value of malt extract depends, for the test is simple and satisfactory, but how far official supervision will eliminate the real purpose of the sale of these products is not yet certain.

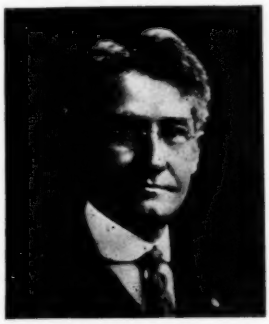
HENRY LEFFMANN.

ORIGINAL ARTICLES

THE CHEMIST AS A DETECTIVE*

By Charles H. LaWall, Ph. M., Sc. D.

THE TITLE OF THIS LECTURE is one which may attract some and repel others. It all depends upon the viewpoint and upon the interpretation of the two principal words—"chemist" and "detective." There was a time when the word "chemist" meant a long-whiskered individual who led a hermit-like existence and whose search for mysterious kinds of knowledge was conducted more or less secretly and with the assistance of a queer looking lot of apparatus. The alchemist, as the practitioner of the art was called, was usually a seeker after the unknowable —the philosopher's stone or the elixir of life, for example.



Charles H. LaWall, Ph. D., Sc.D.

The detective of the older type of fiction was a "gent" with false whiskers and rubber-soled shoes, who carried a gun and who was always ready to flash an official badge at a moment's notice by nonchalantly throwing back his coat lapel.

Nowadays there are as many kinds of chemists as there are varieties of automobiles, and while every chemist is a detector, or one who brings facts to light, there is only a limited number of members of the profession who are qualified by training and experience to cope with the many phases of the science which have to do with the detection and punishment of crime. It is the latter group with which we are particularly concerned upon this occasion—the chemists who are called upon to support some phase of the law, either criminal or statute, and I am sure of interesting at least that part of my audience who are members of the anomalous organization called "The Crime Club," in which membership does not necessarily presuppose criminality on the part of the applicant.

The modern detective novel is a fascinating form of literature to a very large proportion of readers of current fiction, and many

*One of a Series of Popular Science Talks given at the Philadelphia College of Pharmacy and Science, 1930 season.

authors in this field have availed themselves of the possibilities in modern chemistry to make their works more attractive and to provide new thrills. Sherlock Holmes has become a household word, although the original Sherlock, while versed in chemistry, did not often employ it as an important factor in the solution of the mystery at hand. Craig Kennedy is more modern and more scientific in his methods, although his greatest reliance is upon physical apparatus for recording psychological impressions. The creator of Fu Manchu, and the equally versatile and perennially fruitful Edgar Wallace are fully conversant with chemical science and its possibilities in fiction, but no author as yet has more than touched the fringe of the subject; in fact, I venture to say that the official reports of A. Lucas, O. B. E., F. I. C., Director of the British Governmental Laboratory and Assay Office at Cairo, contain more potential plots and more fascinating stories of crime detection by chemical and related methods, than have ever been used by all of the writers of detective fiction from the time of Dioscorides to the present.

"ITALIANATED"

I mention Dioscorides, for while he was not a writer of best sellers of his time, he certainly was the one who first classified poisons and described their effects, though it was many centuries before the analytical chemist appeared upon the scene with his methods for detection and estimation of substances administered for the purpose of destroying human life. And poisons have played an important part in history from the time of Tiglath Pileser to the present. At one period in the history of Italy the practice of poisoning for revenge, profit, or for almost any other reason, may be said to have been pandemic, and the names of the Borgias, the Medicis, and Madame Toffana will be forever associated with toxicology. One of the famous poisons of that time (probably a preparation of arsenic) was called "Powder of the Succession," because it was so frequently used by younger sons in speeding up the acquisition of the title. To be "Italianated" meant to be the victim of poison secretly administered.

Thanks to the researches of modern chemistry, beginning with Orfila, more than a century ago, the proof of the presence of poison is so certain in our time that poisoning is a rare charge or count in a modern bill of indictment for murder, and with some poisons the basic elemental substance is so indestructible that chemical evidence

of the presence of poisoning could be obtained even after the lapse of centuries.

POISONS OF HISTORY

I doubt not that if the tomb of Alexander the Great were to be discovered and the remains submitted to a chemist for examination, it could be determined with certainty whether any of the mineral poisons commonly used at that time, such as arsenic, lead, or mercury, were present, for it will be remembered that Alexander's last illness, which some authorities believe was due to the administration of poison, was of several weeks' duration, which would indicate the use of a mineral poison rather than one of the poisons producing a rapid effect, such as was used with such success by Locusta in the poisoning of Britannicus. In this latter case the poison was probably one of the forms or combinations of prussic acid, which had been known and used from the time of the Egyptians, who referred to its use in the enigmatic phrase "the penalty of the peach," thus indicating a knowledge of the fact that peach kernels contain prussic (hydrocyanic) acid, and also, inferentially, that they were able to prepare this poison in a concentrated form from the source named.

While I do not purpose devoting more than a small portion of the allotted time to the subject of toxicology, it may be appropriate to mention that a Greek writer named Nikander, of the third century B. C., wrote a comprehensive work on poisons and referred to certain complex preparations of drugs as specific antidotes; those which were to combat the effects of the bites of venomous animals or insects were called "alexiterics," while those which were effective against drugs administered internally were called "alexipharmics." The name "theriac," derived from the first of these two words came to be employed for many centuries to designate remedies which were supposedly effective against all kinds of poisons.

Poisons of vegetable origin, such as the toxic plant principles, strychnine and morphine, etc., are not as resistant to putrefactive changes as are the mineral poisons, but their detection and estimation within a short time after administration is usually certain, and taking into account the symptoms preceding death and the observations and opinions based upon a post mortem conducted by a properly qualified individual, poisoning by such substances is usually promptly detected and punished if the investigation is in the hands of competent authorities and is instituted promptly.

It is in connection with such poisons as venoms, toxins, ptomaines and disease-producing bacteria that the chemist is still unable to proceed with certainty, but such methods of poisoning are rare and there are other sciences than chemistry that are helpful in bringing about detection and conviction.

Few analytical chemists are available for or care for such toxicological work as is necessary in connection with poisoning cases. The materials are not pleasant to work with, the chemist often being required to be present when the post mortem is conducted, and the responsibilities are very great indeed. Certain phases of this work, common to all chemical work which is to play a part in court procedure, will be discussed later in detail.

POISON PLOTS

Only one who has had experience as a public analyst can have any conception of the number of individuals in a community who have an idea that they are the victims of poisoning plots. The great majority of these, fortunately, are imaginary cases, but every once in a while the analyst is surprised and astonished at the boldness with which such crimes are attempted. I remember one case in which a sample of a well known proprietary infant food reached me from a nearby medical school to which the sample had been sent by an alumnus of that school who was a practicing physician in western Pennsylvania. The facts accompanying the sample were meagre, but the first preliminary test revealed arsenic, and further investigation showed the presence of a dangerous amount of white oxide of arsenic, commonly available as "Rough on Rats."

A long-distance telephone call acquainted the physician with the facts so that remedial measures might be promptly instituted, and it was then learned that the package had been returned to the doctor's office by the young mother of an illegitimate child, the father of whom had presented her with the package (and had probably added the poison). The young mother, not associating the death of the child with the food, returned it to the physician's office together with some unused medicine, and the physician's wife, seeing this package of baby food on her husband's desk, and noting that very little had been used out of it, took it for her own child, who promptly developed diarrhœa, which is one of the early symptoms of arsenical poisoning.

It is almost unbelievable, yet true, that the physician who sent in the sample which had poisoned his child, refused to pay any fee, nor even the charges for the long-distance telephone call, because, as he said, he had sent it to his own college where they should have done it for nothing, and had not expected them to incur any expense without notifying him beforehand.

Another case of attempted murder was revealed by the examination of some biscuits baked by a young bride for her elderly spouse. The biscuits were brought in by the physician who was attending the elderly man, as he suspected that something was wrong with his patient's food and took a chance on the biscuits. Upon examination they were found to contain over 5 per cent. of white lead which had been mixed with the flour. A very clever attempt, because the symptoms of lead poisoning are not always the same and poison is not always suspected in such cases by the attending physician.

A sample of tea was once handed to a food inspector by a complainant who said that her husband had been ill ever since she had used tea from that package for his meals. As she did not drink tea she picked upon that article of the diet of which only he partook. This was a case of added arsenic, like the baby food case previously related.

Samples of candy which has been maliciously poisoned are occasionally encountered, but the great majority of suspected cases result negatively upon examination of the sample. One positive case, just recently investigated, concerned a single stick of chewing gum handed to a young lady by her boy friend. She suspected it for some reason which she would not disclose. An examination of the sample showed that the white powdered sugar which ordinarily is used on the outside of chewing gum sticks had been replaced by white arsenic.

In another instance bichloride of mercury was found mixed with the sugar in a boarding house sugar bowl, and in still another, calomel was found mixed with the sugar in the sugar bowl on the private table of the landlady herself.

"TOXICOMANIACS"

All of these cases are unfinished, so far as the analyst is concerned, for no criminal charges resulted in any of them and no further facts were communicated to the analyst. There are persons in every community who might with propriety be called "toxicomaniacs," not because they are in the habit of giving poisons to others, but because they are constantly laboring under the

mistaken impression that they are being poisoned. The few cases cited above are but a small proportion of those investigated, but in every sample submitted a thorough and careful examination must be made to avoid overlooking a case which might result in tragedy.

A "NOVEL" NOVEL

In closing this portion of the lecture I should like to remind my hearers that the novel "Stringtown on the Pike," written just thirty years ago by that famous pharmacist and internationally famous scientist, John Uri Lloyd, has for its dramatic climax a scene in which the chemical testimony of an acknowledged authority who had apparently proved the presence of strychnine in the stomach of the victim by a test which had hitherto been considered infallible, was nullified by a self-constituted investigator in the person of a student of chemistry who had faith in the innocence of the accused, and who by a clever series of experiments and deductions from the facts brought out by the defense in the trial, was able to prove that this hitherto infallible test for strychnine was fallacious and that the same reaction could be produced by other common drugs which had been admittedly used for medicinal purposes by the deceased. The story was not only a good one but the statements made in the dramatic climax, when the case was reopened for the admission of new testimony, are all scientifically correct. This is the first time in the history of chemistry that a novel was used as the medium for the original publication of an important scientific discovery. The book created a furore among toxicological chemists at the time of its publication in 1900, but not only were the statements verifiable, but the result has been to discredit what are called color reactions for the identification of alkaloids, unless supported by other chemical reactions.

Many famous criminal trials have been conducted in which the testimony of the chemist has played an important part; among those which attained international prominence in their time were the Maybrick case and the Carlyle Harris case. In the former it was arsenic that was used as the poison, while in the Harris case it was morphine, a capsule containing a lethal dose of this poison having been substituted for a single capsule of the same size and appearance in a dozen capsules containing a harmless headache remedy, the capsules having been filled on prescription. This was as difficult a case as can well be imagined, but Carlyle Harris was convicted.

Next in importance to toxicological cases or those involving poison, are those in which the recognition and identification of blood stains are necessary. The details of such tests are complex and not of popular interest, but I may say in passing that blood stains can not only be identified as such after the lapse of many years, but in addition to a number of general chemical tests there are now biological tests which are specific for the identification of human blood as contrasted with the blood of other animals.

So many possible subjects of interest and importance could be mentioned that it is difficult to decide what phase of the work to take up next. Among these is the subject of explosives—their composition and their effects. A knowledge of this field figures in bombings and also in crimes in which firearms are concerned, where the composition of the projectile and markings on its surface received in its passage through the rifled barrel of the weapon and its contact with the object struck often lead to conviction.

The perfection of the recording of finger prints for purposes of study and classification is largely dependent upon chemical research, both in connection with the powder which is used to make visible the impression and the subsequent photography of the print, for it will be remembered that photography is primarily based upon chemical reactions. In this connection I had a very amusing experience while testifying in a civil case involving the value of phenol which had become slightly discolored while in storage. The judge (now deceased) who was sitting at this particular time was one of Philadelphia's most brilliant jurists, who frequently took the cross-examination out of the hands of counsel and conducted the case to his own liking.

HIS HONOR SEES THE LIGHT

After having testified to the assay strength of the phenol, which was well over 98 per cent. in spite of its dark color, I was asked by one of the counsels in the case what was the cause of the red color. I replied that so far as actual scientific knowledge was concerned the cause was a mystery, and I then enumerated a few of the alleged causes such as the presence of organic matter, the presence of iron, the action of light. At this point I was interrupted by the judge, who shouted at me in a very irascible manner, "Do you mean to stand there in the witness box and tell this court that light possesses the power to pro-

duce chemical changes?" I very modestly and quietly said, "Your Honor, the whole science of photography is based upon the chemical action of light." His Honor took very little active part in the rest of the conduct of the case so far as chemical or physical technicalities were concerned.

Both incendiary fires and fires resulting from spontaneous combustion present problems which may frequently be solved by the aid of chemistry, for all combustion is a chemical reaction and certain substances often used by those who commit arson are usually detectable by chemical tests, unless the building or room is entirely destroyed.

GROUND GLASS HYSTERIA

In going over this miscellaneous list I am reminded by the fact that in the early days of the war when suspicion was rampant in connection with the alleged poisoning of foods, many glasses of perfectly good grape jelly were sent in to be examined for the presence of ground glass. The complainant would triumphantly point out the particles of glass (?) which were visible when the container of jelly was held before a strong light, and no amount of explanation would suffice at times until the chemist would carefully separate some of the particles in the presence of the complainant and show by a very simple demonstration with hot water and a test tube, that the so-called glass was soluble, which real glass of course is not, and that the substance under suspicion was really cream of tartar, which frequently separates out in a glass of grape jelly in the form of small transparent, sharp crystals.

One large manufacturer of breakfast cocoa during this same hysterical period came in to the laboratory with several samples of his product which were apparently normal in appearance and in flavor, but which upon cooking made a dark beverage of repelling appearance. Sabotage or tampering with the product by an alien employee was the thought in the mind of the manufacturer. An analysis of the cocoa showed the proximate constituents to be normal except for the fact that the color of the ash obtained on ignition indicated the presence of an abnormal amount of iron as indicated by the color of the ash. This in itself was not much to go on, but a lucky "hunch" led to the passing of a magnet through some of the original powder, to find upon its withdrawal that it had adhering to

it innumerable microscopic particles of metallic iron. What was the source of this iron? A nail or a number of nails had found their way into that particular lot of cocoa beans, and when they entered the mill the iron was pulverized and the particles disseminated throughout the lot of powdered cocoa. The installation of a set of magnets in the feed hopper of the mill to attract and remove iron nails and other iron particles not only removed the difficulty, but the daily catch of nails and bits of iron convinced that particular manager not only that his suspicions concerning sabotage had been unfounded, but that certain occasional defects in the uniformity of his product had been due to this same cause, which might never have been discovered had it not been for the fortunate (in this case) contamination with an unusually large proportion of iron.

CANDY ANALYZED

I had a very amusing yet costly experience some years ago when a candy manufacturer sent me a large sample of candy which had been made in a steam kettle near which an electric light bulb had burst and in which he feared some particles of glass might have found their way. The whole five-pound sample of the candy (it was a pure sugar candy) was dissolved in a sufficient quantity of water and the entire solution was filtered so as to catch any particles of glass that might be present. I carefully examined the residue on the filter for glass, but found none. I did find, however, the following list of foreign particles identifiable by microscopic examination: Fragments of wool, cotton and linen fibres, two varieties of wood fibres, cornstarch, yeast cells, several fragments of cigarette tobacco, fragments of wings and legs of insects, fragments of human hair, and of several kinds of paper.

In writing my report, besides stating that no glass fragments were present, I was tactless enough to give the list of things that I had found and to suggest that the factory had better be kept a little cleaner or the pans protected from dust, for of such miscellaneous character are dust particles composed as found on exposed articles or surfaces. I lost the client, who had frequently called upon me for analytical services. He didn't like my report, even though it was favorable as far as his original inquiry was concerned. After several years' absence, however, he returned and has since then seemed satisfied with the reports, but he has never again sent in any large samples to be examined for glass.

A POUND OF RAISINS, ETC.

When we were fighting for legislation some years ago to compel the covering of foods and beverages that are exposed to street dust, I had a prize sample of a pound of table raisins that were purchased from a street stand, and I still remember the effect that this report had upon a legislative committee before whom I had been called. The raisins were fuzzy with street dust. Besides the raisins I found all of the following:

Prunes, very dirty.

Beans.

Rice grains.

Dirt so thick on upper surface that the raisins looked fuzzy; numerous hairs visible.

Microscopic examination showed the following:

Hairs, human and animal.

Fragments of animal and vegetable fibres, cotton, wool, etc., dyed green, blue, yellow, brown, pink and gray.

Partly disintegrated bast fibres similar to those from straw, probably from manure.

Partly disintegrated bran fragments, probably from manure.

Sand.

Cornstarch, rice and wheat fragments.

Spores of yeasts and molds.

Pine wood fragments.

Fragments of three other unidentifiable woods.

Unidentifiable vegetable tissue containing spiral ducts.

Tobacco leaf fragments, probably from cigar butts.

Fragment of yellow stained cigarette paper.

Fragment of charred cigarette paper.

Fragment of cigarette tobacco.

Fragments of wings and legs of insects.

Another of the war time activities of the detective chemist was in connection of the enforcement of the regulations of the United States Food Administration when the nation was trying to conserve wheat in the effort to help feed the allies. These regulations were prohibitive as regards the use of unmixed wheat flour in bakery products. In fact, for this particular emergency our food laws relating to such products were literally turned upside down, and practices which were then made mandatory, were before and have been since that period, punishable under the food adulteration laws.

BOOTLEG BREAD It was amusing to see how many bakers in Philadelphia refused to adulterate their products, their resistance not being based at all upon moral grounds, but upon the desire to serve their customers with the pure wheat products to which they had become accustomed, for as a matter of fact, the public did not like the foods made with the mixed flours and there was much clandestine making and serving of pure wheat articles, "bootlegging bread," as we might appropriately describe it.

Now, to the food chemist the use of the microscope is a part of the daily routine, for microchemical tests play an important part in many of his investigations. Starches from different grains and cereals are markedly different in appearance under the microscope, and the accidental presence of other distinctive tissues makes it possible to detect with certainty the admixture of one flour with another, and a trained microscopist can determine the proportions of different ingredients with a fair degree of accuracy. The bakers who attempted to evade the regulations did so clumsily and were almost invariably detected and penalized.

One of the clever points in the handling of these cases was the fact that after a hearing had been held in the regulation legal manner, at which one of the food officials acted as judge and the defendant was permitted to have counsel and call witnesses, if the decision was "guilty" (and 90 per cent. of the defendants plead guilty after the first week's hearings), a fine was imposed in proportion to the size of the batch involved and whether it was a first, second or third offense, the fines were made payable to the American Red Cross, and the treasury of that worthy organization was augmented by many thousands of dollars in Philadelphia alone during the last year of the war.

THE FOOD CHEMIST Now in these cases the story might have been different had a trained chemist supervised the mixing. In fact, there were formerly many branches of the food industry when the only use the establishment had for a chemist was to aid in systematically and intentionally violating the law, and for some years it seemed as if the violation advisory chemists were a few laps ahead of the law-enforcing chemists, but such is no longer the case.

This brings us naturally to the role of the chemist in detecting violations of the food adulteration laws, for such laws would be unenforceable were it not for the services of chemists who are ex-

perienced in that field. The responsibilities of the chemist in this connction are two fold: first, in the analysis of many samples of normal food products and establishing of standards of purity; second, in the devising of methods of detecting adulteration. In some instances the method of proving the presence of an adulterant is simple and positive; in other cases it is extremely complex and difficult. For example, as small a quantity as one teaspoonful of formaldehyde in 100 gallons of milk may be detected with certainty, although this amount is too small to be effective as a preservative,* while a modern, up-to-date complete report of the analysis of so simple a substance as cider vinegar is almost as complicated as an income tax report, and requires a gallon of vinegar and about two days' time to complete.

Thanks to the united and sincere efforts of national and state food law enforcement officials, aided by experienced chemists and inspired by the stimulating example and leadership of Dr. Harvey W. Wiley, practically all of the flagrant and harmful forms of adulteration formerly encountered have entirely disappeared. This does not mean that the battle is over. The general statement is intended to apply particularly to nationally distributed products or products entering interstate commerce where both state and federal authorities can join hands in the work of suppression. In some lines there is nearly as much adulteration as was formerly the case, but it is all of local origin and can be combated only by state and local authorities.

Some of the forms of adulteration in which the chemist's services are important and indispensable are as follows:

MILK ADULTERATION

Milk and cream were frequently found to be not only watered and colored, but were found to be preserved with formaldehyde or borax. The preservatives were used to save the cost of ice. In fact, formaldehyde solution was supplied to milk dealers at a fancy price under the suggestive name of "Iceline." In consequence of the rigid and continuous enforcement of federal, state and local laws affecting milk and cream, there are a few instances of recent years where milk or cream has been found to be tampered with. Butter, however, is still frequently found to be grossly adulterated with water. The legal limit of water is 16 per cent. Butter made by reliable creameries

*This test requires but a teaspoonful of milk and a few minutes' time to perform.

usually contains from 10 per cent. to 14 per cent. of water, and butter churned under normal conditions always falls within this range. A butter maker who knows the trick of incorporating excessive amounts of water in the butter can raise the water content up to 30 per cent., without materially changing the appearance or consistence of the butter, and we have had samples in the Philadelphia market containing as high as 38 per cent. of water—a tidy profit for the creamery that can get away with it. There once was a time when oleomargarine was largely sold for butter. Such substitution is now exceedingly rare, as oleomargarine has found its proper place as a butter substitute, openly sold as such.

There are very many comprehensive and detailed laws affecting beverages of all kinds. As an example of how well these laws cover the subject I can cite a case in which a sample of lemonade was purchased from a street vendor. Taking into account the conditions under which this lemonade was dispensed, part of which are under the jurisdiction of the inspector and with which the chemist has nothing to do, this sample was found to be illegal on five counts, which were as follows:

ALL FOR FIVE CENTS

1. It was sold from an uncovered container.
2. It contained ice, floating in the beverage itself instead of surrounding the container.
3. It showed a deficiency of lemon juice.
4. It contained saccharin instead of sugar.
5. It contained a poisonous amount of zinc from its having been made in a galvanized bucket.

This would seem to be quite sufficient for a five-cent glass of lemonade.

Vinegar is frequently sold in violation of the law, not so much on account of the presence of harmful adulterants but because in place of the more expensive cider vinegar one of the cheaper varieties has been substituted wholly or in part.

Olive oil is occasionally adulterated with cottonseed oil or other cheaper oils, but the number of such violations is a small fraction of that found several decades ago.

Preservatives in general have gone out of use, partly due to the enforcement of the food laws, but more generally due to the improved sanitary conditions which obtain in food packing establishments.

SODIUM BENZOATE

When the Food and Drugs Act was passed there were only one or two tomato catsup manufacturers who put up their products without preservatives, claiming to rely upon the soundness of the materials used and the maintenance of rigid sanitary conditions in their plants. By far the greater number of manufacturers claimed, at a congressional hearing in 1910, that it was absolutely necessary to use sodium benzoate, which was then made one of the few permitted preservatives when used in a limited amount. Sodium benzoate was then selling at about sixty cents a pound. When, during the war, the prices of certain chemicals, usually obtained from Germany, soared to almost incredible heights, and when the price of sodium benzoate advanced to more than eight dollars a pound, it was remarkable how many manufacturers of tomato catsup, who had claimed that it was indispensable, found that they could do without it and have never gone back to it.

TRICKS OF THE TRADE

It is not generally known in this country that adulteration or substitution is frequently controlled in European countries by the intentional addition to certain articles of food and drink, of substances whose recognition by chemical or microscopical tests is extremely simple for the analyst or inspector. For example, potato starch is required to be added in very small amount to oleomargarine, at the time of its manufacture. Now, potato starch may be recognized by a microscopic examination which may be made by a trained inspector using a pocket microscope, or the presence of starch, generically, may be recognized by the same inspector by a very simple chemical test made in the presence of the seller. This effectually prevents the sale of oleomargarine for butter when efficient inspection of markets and stores can be maintained. In some countries which do not use the potato starch method of control, an easily identifiable fixed oil like oil of sesame is required to be added. This, too, can be quickly detected by the inspector.

Almost everybody nowadays is familiar with the name "phenolphthalein," for it is used as a laxative ingredient in petroleum oil emulsions, in chocolate blocks or other laxative confections and in laxative chewing gum. Few persons know, however, that the properties of phenolphthalein as a laxative were not discovered until many years after its introduction as a laboratory reagent. It belongs to the group of reagents known as indicators,, which substances have the property of showing a change in color at the conclusion of a chemical

reaction. Phenolphthalein is colorless in acid solutions, but develops a brilliant red color in the presence of a small excess of alkali.

In Austria there are many fine varieties of grape wine, all of which have their imitations. In order to control the practice of substituting imitation wines for real wines the Austrian authorities required the manufacturers of the spurious wines, which had a perfectly legitimate market if sold honestly for what they were, to add a small quantity of phenolphthalein to these imitation products so that the inspectors of food and drink might with quickness and certainty distinguish by a simple chemical test between the genuine and the spurious. Shortly after this regulation went into effect the habitual drinkers of these spurious wines complained of continual diarrhœa, and upon investigation of the cause, the harmless laxative properties of phenolphthalein were thoroughly established and where ounces were manufactured in the past, hundreds of pounds are made today.

HOT PEPPER

An American employment of a similar indirect method of establishing the proof of an adulteration of pepper was the result of a startling and dramatic finale to a Federal prosecution some years ago. A well known firm of spice importers and sellers was prosecuted under the provisions of the Food and Drugs Act for having adulterated their ground black pepper with pepper shells. It so happened that they were importers of pepper shells, which have certain legitimate uses. The United States authorities, suspecting the illegal diversion of some of this imported material, had impregnated the shipments received by this particular firm with traces of an easily recognizable chemical which was harmless and which was easily identified in very minute quantities. After the accused firm had established what seemed to be a very good defense, through the efforts of its scientific staff, the United States authorities called in their chemists to testify to the presence of this particular foreign chemical in the defendant's pepper, and the defense wilted.

WATER SUPPLIES

Another fruitful field of work for the detective chemist is in that of water supplies and water contamination. Here it is customary for the chemist either to work hand in hand with the bacteriologist or to be trained

in that field himself, which is preferable. An interesting and somewhat spectacular phase of such work is the tracing of sources of contamination of wells, reservoirs or springs. There are certain substances that can be added to a suspected source of pollution, such as a cesspool, which by communicating some specific property to water which it does not ordinarily possess, will appear as a distinctive factor in a well, spring, or reservoir, if there is any subterranean connection leading from the cesspool thereto.

One such substance is kerosene, which if, when added to a cesspool, appears in the suspected water supply with its characteristic odor and flavor, proves conclusively the source of contamination. Another method is to add to the cesspool a chemical dyestuff known as fluorescein, which communicates to the water in the well, reservoir, or spring, a startling green fluorescence, which, while perfectly harmless in the amount used, is alarming to the users of the water.

Sometimes a large amount of salt is added to the cesspool, having previously determined the normal salt content of the water supply. Still another method is to introduce into the cesspool a chemical not usually found in drinking water, such as a salt of lithium, which may be detected by means of an instrument known as the spectroscope, the most delicate testing instrument known. The first and second methods described are the best to employ, for they usually bring about immediate cessation of the use of the contaminated water.

NARCOTIC CHEMISTRY

Another group of laws in which the trained chemist's services are indispensible are those connected with the control of habit-forming drugs. The most important of these drugs are opium and its principal derivative, morphine; cocaine, the alkaloid obtained from cocoa leaves; heroin, an artificial alkaloid related to morphine; and cannabis indica, also known as hasheesh, from which our word "assassin" is derived; this drug is also known to its devotees as "guaza," "bhang," and "marihuana."

COSMETIC CHEMISTRY

There is one group of substances for which no controlling laws as yet exist, concerning which the chemist is frequently retained in private damage results. These are the cosmetic preparations, of which the great majority are free from suspicion altogether, but there are two small groups in which harmful constituents are frequently found. These

are the hair dyes and the freckle removers and skin bleaches. I have seen cases where the user of a hair dye suffered from a very unsightly and painful skin disease because of the presence of a chemical to which the user was particularly susceptible. Such susceptibility is called an idiosyncrasy, and no damages can be collected, as a rule, no matter how severe the injury.

Then we have the lead-containing hair dyes, whose users may not show any symptoms until enough lead has been absorbed to bring about a distressing condition known as chronic lead poisoning. The freckle creams frequently contain injurious amounts of mercury compounds. But a certain number of women, in their desire to make or keep themselves attractive, will run any risks, however dangerous.

DETECTION OF FORGERIES

Another fertile field for chemical services of great importance is that of false or fraudulent documents and letters. Here not only can the identity of the paper be established by microchemical tests, but by establishing such identity the period in which such paper originated is automatically proven. Prior to the ninth century vellum or parchment was used throughout Europe almost exclusively, paper not yet having been introduced from the Orient, and the use of papyrus having been practically confined to Egypt. Then the chronological periods of successive types of paper appear in the following order with the accompanying approximate dates: linen rag paper, ninth century; cotton rag paper, eleventh century; straw paper, 1800; wood pulp paper, 1840; esparto paper, 1860.

Inks likewise have their approximate dates of origin and may readily be identified by chemical tests. The earliest inks were carbon inks, or inks made from colored pigments held in suspension. The iron tannate, or nutgall ink, as it is commonly called, originated in the eleventh century; the indigo inks and the logwood inks in the eighteenth century, while the coal tar inks were not in use until the latter half of the nineteenth century.

Methods of staining papers by steeping them in coffee and similar decoctions to give them a fictitious appearance of age yield products which are also readily detectable by chemical means. An individual, therefore, who tried to palm off upon a purchaser of autographs, a holograph letter, let us say, of Queen Elizabeth, and who had written it with aniline ink upon wood pulp paper stained with coffee, would be out of luck if a chemist were called into the

case, and instances of many such exposures are a matter of record and attempts at such deceptions occur not infrequently.

Besides the chemical methods for detecting evidences of alterations in documents, there are physical methods, such as the use of ultra-violet light. This phase of criminological work will be discussed at a later lecture in this series by my colleague, Dr. Sturmer.

It is a matter of interest, too, to know that graphite pencils date from about the sixteenth century, prior to which time metallic lead styluses were used for writing on paper, hence the erroneous name "lead pencil," which persists after three centuries of use of a substance other than lead.

Alterations or erasures in handwriting itself and even the sequence of strokes are demonstrable by microchemical tests, and the field of invisible inks (sometimes called sympathetic inks) for secret writing, is a chemical problem from beginning to end, and the use of such means of communication played an important part in the secret service work of all of the participating nations in the World War.

The identification of cloths and fibres is another important field of detective work for the chemist, as is the detection of counterfeit bank notes and spurious coins.

One of the recent bits of chemical research which aids in the identification and recovery of stolen automobiles is rather remarkable. Although the engine number of a car, which in many cases is stamped into the metal of the engine body by pressure, may be filed away and an entirely new and different number stamped in its place, the original number may be brought out with distinctness by exposing the area involved to the action of certain chemical vapors.

I think that by this time I have covered a sufficiently large field and given enough examples to prove that the chemist may very well be classed as a detective in connection with law enforcement although he does not don gum shoes and false whiskers as the fiction detective used to do. Even a knowledge of the composition of dust and dirt may play an important part in the detection of crime, much in the same way in which such data were used by the versatile Sherlock Holmes. But there is this important difference between the chemist as a detective and the private or official member of the orthodox crime detecting fraternity. The chemist has extra responsibilities in connection with the receipt and custody of the sample or samples, and he is not only a witness in the ordinary sense but actually acts as an expert witness as well.

THE EXPERT

In discussing this phase of the subject I would like you to disregard several humorous definitions of an expert witness. One of these is that the expert witness is a professional man away from home; the other draws an unpleasant comparison between liars, damned liars, and expert witnesses. Another reproach is in connection with the definition of a specialist as one who knows more and more about less and less. This is not true of the detective chemist, whose field of work is broader than that of any other in the profession and who must also possess imagination and a knowledge of thousands of unrelated facts, any one of which may help give the clue to the problem for whose solution he is searching. This field of chemistry in the service of the law is sometimes called "forensic" chemistry.

It must always be remembered that the burden of proof is on the accuser in a criminal or other legal prosecution. The chemist, of course, may figure on the side of either the prosecutor or the defendant. He deals with facts primarily, scientific facts, of course, that are capable of proof, and on the basis of these facts he may make deductions and express opinions, this constituting him an expert witness and distinguishing him from the ordinary witness who is confined to facts only and who may not make deductions or express opinions. This is a great responsibility in itself and the chemist who lives up to the ethics and ideals of his work will never be a partisan but will give his testimony impartially and without bias.

One of the most important factors in chemistry as it pertains to the criminal law is the sample or specimen taken for analysis. The collection of the specimen or sample is not often under the jurisdiction of the chemist. When it is not, the transfer of the sample must be made in person and not through an intermediary. The chemist, as the custodian of the sample or specimen, must then keep it in such a manner that it may not be tampered with until he appears with it at the trial of the case. In other words, there must be no lapse of continuity from the time the specimen is taken until it is offered in evidence.

An interesting story is told of a certain district attorney who had been charged an exorbitant fee by a chemist with whom he had not made an agreement before the trial as to his charge for his services. The chemist and the district attorney, it may be said, lived at opposite ends of a large state. Several years thereafter the district attorney sent one of his assistants to this same chemist with an important specimen which was connected with a case of alleged mur-

der. After the preliminary discussion of the case, and after the chemist had stated what his fee would be for the analysis of the specimen and attendance in court, the messenger casually asked the chemist if he would keep the sample until he, the messenger, went back to the hotel and discussed the fee with the district attorney. The chemist consented, and after an hour or so the messenger returned and said that the price was too high and asked for the return of the sample which he took back to the district attorney, who then made satisfactory arrangements with another chemist. When the case came to trial the first chemist was surprised to receive a summons, not as an expert witness, but as an ordinary witness whose testimony was needed to prove the history of the sample, and for which he would be entitled only to mileage and a nominal witness fee. It was a bitter pill for the chemist to swallow but there was no evasion possible, and he had to spend three days in traveling and court attendance for bare expenses in order that he might account for the custody of the sample for a single hour.

The chemist must know, not only how to analyze the sample, but he must also be cognizant of certain chemical changes which might take place in a sample between the time of its collection and its delivery to the chemist. In samples of suspected beer, for example, where the alcoholic content might increase, it is now customary for the agent who collects the sample to place a bichloride of mercury tablet in each bottle of alleged beer before sealing it, thus precluding the possibility of the sample increasing in alcoholic content before its examination by the chemist, which would be an injustice to the defendant. It will be realized that a chemist's samples are not to be recklessly tasted.

The chemist is responsible, of course, for the decision as to the character of the analysis, and also for the selection of the method or methods to be followed. Without going into the technical details it may be stated that an analysis may be proximate or ultimate, partial or complete, direct or indirect. Most analytical methods have been standardized and are recognized as authoritative. Many occasions arise, however, when the chemist must improvise or develop a new method, which entails some preliminary research, and he must be prepared to defend this method in detail upon cross-examination.

It must be remembered that in giving his direct testimony, as well as in cross-examination, the chemist must testify in non-technical

language as far as possible, not only for the sake of the jury but for the judge and attorneys as well. It will always be found that the chemist who succeeds best in this difficult task is the one whose services are most frequently in demand.

The chemist may also use his detective ability and frequently does so in civil cases, such as those involving patents and their claims, breach of contract for supplies sold on specifications, accidental injury from incorrect filling of a prescription in a pharmacy, or poisoning from unwholesome food consumed in a restaurant or hotel. There is no single group of chemists in this country corresponding to the Public Analysts of Great Britain, who are the most highly trained (and poorly paid) group of public servants in the world.

Utilization of the possibilities, not only of chemistry, as has been outlined in the foregoing, but of all scientific methods, is being made in Berkeley, California, by Chief of Police Vollmer of that city, who has made an international reputation for the systematic and continuous use that he has made of scientific methods in the detection of crime. Chief Vollmer has personally reorganized the police departments of a number of cities in our country and also in Havana. He is now conducting a course on his methods in the University of Chicago, a department which is called the "School of Criminal Investigation."

An American pharmaceutical chemist, who I am told was a friend of Chief Vollmer, and who devoted much of his scientific ability in aiding in the detection of crime up to the time of his death less than a year ago, was Professor Albert Schneider, of the School of Pharmacy at Corvallis, Oregon.

One of the most splendidly equipped laboratories in the eastern part of the United States for the work of scientific crime detection is in our own new city morgue, and is under the direction of Coroner's Physician Dr. William S. Wadsworth, who is a brilliant example of an internationally known scientific expert engaged almost entirely in crime detection. The Nestor of detective chemists in this section of the country, at least, is Dr. Henry Leffmann, whose knowledge of the subject is remarkable and whose experiences would inspire many interesting books, and who is also internationally known as a chemical expert.

There is more widespread recognition of the important relation between science and the detection of crime in European countries

than in America. For more than a score of years courses in "Criminalistics" have been given in the Universities of Prague, Bucharest, Lausanne, Liege, and other prominent universities. A dozen or more individuals in Europe have international reputations as scientific criminologists, and the criminal investigation department of Scotland Yard, known to readers of detective fiction as C. I. D., is very much up to date in scientific methods applied to criminology. The Parisian Surete stands equally high in this field and the great Alphonse Bertillon was officially connected with the Department of the Seine as anthropometrist in particular and scientific expert in general, for his testimony in connection with the authenticity of documents was an important factor in the celebrated Dreyfus case.

ENTERIC COATINGS*

By Milton S. Wruble, B. S., M. Sc., Philadelphia, Pa.

I. Study of Some of the Possible Enteric Coatings.
II. Study of Shellac as an Enteric Coating.
III. Survey of Manufactured Enteric Coated Tablets.

Object of Problem

THE PROBLEM DEALING with the enteric coatings of tablets was undertaken with two principal objectives in view, (1) a study of the value or effectiveness of the more important coatings already in use and (2) the development of a new coating suitable for large scale production.

It has generally been conceded that no enteric coating in present use is entirely satisfactory.[1] Scoville says, "The really ideal coating for enteric purposes has not yet appeared, and the matter is still to be handled cautiously." In a recent article by[2] F. O. Taylor, the author expresses the same views.

Most of the common coatings were studied in this work with the exception of (1) Keratin, because enough evidence was found in

*Thesis work submitted to the Faculty of the Philadelphia College of Pharmacy and Science as partial solution of a problem kindly submitted by Eli K. Lilly & Co., Indianapolis, Ind. Results are of the nature of a preliminary report.

[1] "The Art of Compounding," W. L. Scoville.

[2] *American Druggist*, January, 1930, page 82.

the literature to show its unsuitability and (2) Stearic acid, since this material does not lend itself to large scale coating and (3) glutoid or gelatin capsules immersed in formaldehyde solution, because the enteric properties of this substance change.

Introduction

An enteric coating is one which will withstand the acid fluids of the stomach contents, remaining intact and which will then pass on and dissolve in the alkaline intestinal fluids.

The ideal coating would, of course, be one which would withstand the attack of the stomach contents indefinitely and immediately be attacked and broken up upon entering the intestinal tract. While such rigid restrictions are not met with in the human system, as a practical specification, an enteric coated tablet should withstand the stomach fluids four hours and be deprived of its coat within one-half hour after entering the intestinal tract.

The ideal coating should also possess certain physical properties. It must be entirely impervious to the fluids with which it is in contact. It must be free from brittleness since during the process of peristalsis it would tend to break off. It must have no medicinal action of its own and of course not be toxic.

The first portion of this work was entirely devoted to the study of spraying enteric coating solutions. It was thought that at least in the case of salol, the spraying of this substance dissolved in a volatile solvent, would overcome its objectionable brittleness as well as other objectionable features so well known to those who have tried coating with this substance in the usual manner.

The problem was, therefore, attacked much in the way the paint industry studies the drying of paint oils, thinners, etc. Glass plates about 10 inches by 5 inches were used and upon these were sprayed the various solutions of salol dissolved in volatile solvents. In each case the films were allowed to dry and were examined. The rapidity with which the film dried, then toughness and crystalline structure were observed in each case. It was hoped to overcome the objectionable brittleness of salol by the addition of certain gums or resins which would render the material less crystalline and more plastic.

I

Saturated solutions of salol in ether were prepared and a series of experiments run by spraying such solutions after the addition of

varying percentages of balsam of Peru, gum mastic, rosin and balsam of tolu. The following results were observed in each case, the plates being sprayed with the solutions in a thin film and allowed to dry spontaneously.

Per cent.	*Balsam Peru*	*Mastic*
5	Crystallization almost as rapid as use of straight salol but crystals not as coarse.	Crystallization rate delayed. Smaller crystals than salol alone.
1	Results similar to above.	Results similar to above.
3	Rate of crystallization slower but of same size as above.	Delayed crystallization. Finer crystals.
5	No crystallization and no drying of films after 24 hours.	Smaller crystals. Rate much delayed.
10		Film remained greasy after 24 hours.

Rosin and balsam of tolu used in the same proportions and in the same manner showed practically similar results. The use of this procedure was for the purpose of studying the character of the various films before actually attempting to coat tablets, thus saving time and expense.

Later in the work spraying was attempted once more with the use of volatile solvents by spraying directly into the coating pan. The results were entirely unsatisfactory since the tablets coated very unevenly. The process was changed from time to time but the results showed that the flattened sides of the tablets were becoming coated and the ends were not.

Salol was now used in the molten state as outlined in the National Formulary method, rotating the tablets successively in several evaporating dishes. Good coatings were obtained by this method as long as the temperature of the salol was watched carefully.

The British Pharmaceutical Codex recommends the following coating:

Salol	20.0	4 oz.
Shellac	30.0	6 oz.
Ether	30.0	6 oz.
Absolute alcohol to	100.0	20 fl. oz.

The directions are: dissolve the salol and shellac in ether and alcohol. Tablets were rotated in an evaporating dish with this solution and allowed to dry. The coating failed to display the physical properties necessary and its use was abandoned.

Gluten is a protein obtained from wheat flour by washing with water in which it is insoluble. The resultant product is of a somewhat doughy, elastic consistency.

This mass was dried down to hardened flakes at a low temperature. Its solubility was tried out in the artificial gastric acid intestinal fluids, which follow later in this work, and repeatedly found to be useless as far as enteric properties are concerned. Further work with this material, adding substances to increase its coating properties, studying its chemical nature, etc., still proved to be of no avail.

Along with gluten, the writer investigated *casein,* also protein in character. A purified form of this was obtained and a search through the literature revealed that it is unaffected by dilute acids but hydrolyzed by certain weak alkalies. Its solubility was tested as before in the artificial gastric and intestinal fluids and discarded because of insolubility in both.

Calcium resinate was prepared by melting rosin and adding the required weight of lime. The lime neutralizes the free acids in rosin and forms a substance which is very brittle in character. Its solubility was tested as in the other cases and found to be insoluble in both digestive fluids.

Egg yolk was next investigated because of its lecithin content, the probability being that it might display enteric properties. The yolk was dried down to scales at a very low heat. It was found to be easily soluble in both digestive fluids.

Calcium oleate, after preparation and solubility determinations, was also discarded because of its insolubility in both fluids.

Collodion was used to coat tablets but found to be unsatisfactory because of its insolubility in the digestive fluids.

In all solubility determinations involved in this study, the following artificial gastric and intestinal fluids were used as recommended by Toplis in his work with stearic acid coatings.

Gastric Fluid

NaCl	.14%
HCl (36%)	.25%
Pepsin	.32%
KCl	.05%
$CaCl_2$	.006%
Water	99.44%

The intestinal fluid was that laid down in the Pharmacopœia among the tests for pancreatin.

Intestinal Fluid

Pancreatin	28 gm.
$NaHCO_3$	15 gm.
Water	100 gm.

Fig. 1—Complete Assembly of Equipment.
A. Coating Pan. B. Constant Temperature Bath. C. Motor. D. Dryer. E. 150-Watt Electric Bulb for Maintaining Constant Temperature.

[1] "While it is true that the above-described liquid is not identical with the pancreatic fluid of the intestines, it is reasonable to believe

[1] Toplis, *Proc. P. P. A.*, 38, 1915, 262.

that its digestive power is not greater than the natural secretion nor yet is it more alkaline."

The actual solubility determinations were carried out in a constant temperature bath (see Fig. 1-B), test tubes containing the test tablets being clamped to a revolving disk (Fig. 2-A) making about twelve revolutions per minute.

The water was kept constant at 36 degrees to 37.5 degrees C. by means of an electric bulb and conditions were duplicated as far as possible to simulate those in the human body. The test tubes were examined at certain fixed intervals and the character of the tablets noted.

II

By far the greater portion of the year was devoted to the study of shellac, the writer feeling that its wide use warranted such investigation. It was understood that a number of the large concerns manufacturing enteric coated tablets were using shellac or modifications of this substance.

Shellac requires an animal for its production, thus differentiating this resin from other natural resins. Chemically shellac consists largely of esters of aleuritic acid whose formula is: $HO.CH_2(CH_2)_5.CH(OH).CH(OH).CH_2COOH$. Red coloring matter, wax and moisture make up the other constituents. Tschirch classes it as an aliphatic or fatty resin in which the substances of the fatty series predominate. His analysis of stick lac is: Wax 6 per cent., lac dye 6.5 per cent., resin 74.5 per cent., residue 9.5 per cent. and water 3.5 per cent.

Shellac varnish is directed to be made in the following manner: Place a gallon of alcohol in a clear earthenware jar of two gallons capacity and at the close of the day's work, gently drop into this 3 or 3½ pounds of flake shellac, cool and let stand until the next day. Then with a clean wooden rod stir it for a few minutes and during the day stir it for a minute at a time, one an hour or so and before night it will be dissolved.

The writer used in this work a specially refined bleached shellac, which was free from arsenic. Solutions were made using various proportions of shellac in 95 per cent. alcohol. The best proportion and the one finally used followed that as outlined under shellac varnish. Heat was used to dissolve the shellac at first, with no real advantage except that it hastened solution at the same time wasting

solvent. Absolute alcohol was also tried but with no real advantage. Ether along with alcohol caused a precipitation of some of the constituents of shellac.

Shellac is not only soluble in the common alcohols but also readily soluble in ammonia water, aqueous solutions of borax and the carbonates of soda and potash.

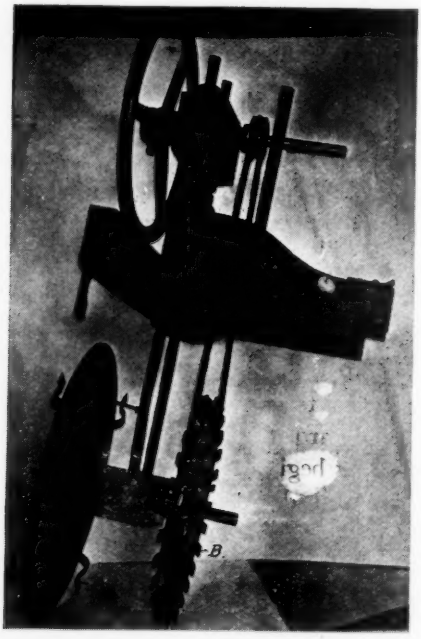


Fig. 2—Interior of Constant Temperature Bath.
A. Clamps for Test Tubes. B. Ribbed Pulley for Agitation.

Ammoniacal solutions of shellac were experimented with since it was found that the free ammonia was entirely volatilized during the coating process. Subsequent immersion of tablets coated with these solutions in phenolphthalein showed no coloration. Ammonia was, therefore, to be desired over the others because of the toxicity point of view.

U. S. P. ammonia water (assaying 29.4 per cent.) was diluted down to approximately 10 per cent. and added to the shellac in a closed container, allowing it to macerate. Solution was complete in twelve to sixteen hours. The shellac was found to change in solu-

bility by exposure, a property which bleached shellac has. Twenty to 25 per cent. by weight of shellac was dissolved in making up all similar solutions.

A small coating pan similar to those used by manufacturers and geared to run twenty-two to twenty-five revolutions per minute was employed in the shellac study. The coating process is lengthy and must not be hurried if it is to be done properly. The tablets are first examined carefully. Those broken are rejected and loose powder sifted out. They are then placed into the pan and a small amount of talc is rubbed through them thoroughly with the hands. The pan is then started rotating and the tablets in this way take up any excess talc that may be present.

After rotating for a few minutes a blast of cold air is blown into the pan. This tends to cool the tablets as well as to blow out any excess talc. A measured quantity of coating solution determined by judgment is thrown over the tablets in such a way as to distribute it over the entire mass, *i. e.*, with a sweeping movement of the forearm. The last portions of the solution strike the back of the pan and slowly drip down.

The air is shut off, the operator standing in front of the pan watching the tablets roll around, and just as soon as sufficient solvent has evaporated off, they begin to mass into balls and to stick to the pan itself. At this point the operator proceeds to break up these masses and to remove those sticking to the sides.

The tackiness of shellac lasts for just a short time, and as soon as it is observed that this period is completed, air is directed on the tablets which are now rolling freely. The tablets are allowed to roll in this manner until the coat is absolutely dry.

The important points observed by the writer in such coating using either the alcoholic or ammoniacal solutions are:

1. Large quantities of tablets must be coated at one time.
2. The tablets must be separated from each other and from the pan at the proper point in the process.
3. The air must be regulated and applied at the proper time.
4. Each coat *must* be dry before applying the next one.
5. Best results are obtained by applying too much coating solution rather than too little.
6. The tablets must be of the proper consistency, hardness and thickness suitable for coating.

7. The coating solution must contain some readily volatilized solvent so as to prevent any undue penetration into the tablet mass, thereby softening it.

Pan coating was carried out with a large number of shellac solutions using mainly alcohol (95 per cent.) U. S. P. ammonia and ether. Ether was early discarded because it was found to precipitate out some of the constituents of shellac and thus did not give a good suspension.

Ammoniacal solutions gave far superior enteric coatings over any other employed. Twenty-five per cent. solutions of shellac in ammonia U. S. P. were made up and tablets coated. The ammonia penetrated the tablets and even though the process was modified by the use of heated air for drying and use of sub-coatings, this penetration could not be entirely overcome.

The same percentage strength of shellac solution was then made up but this time diluting the U. S. P. ammonia with distilled water to approximately 10 per cent. strength. Tablets coated with this solution were not as readily penetrated although the coating process was lengthened as it required longer drying periods with the hot-air blast.

The proportion finally found to give best results was a 25 per cent. shellac solution in equal quantities of alcohol and ammonia (U. S. P. strength), allowing the shellac to dissolve by maceration at room temperature. A comparison of the results obtained with shellac coating solutions follows in tabulated form. These are based on repeated trials and the solubilities were observed in the constant temperature bath with tablets of equal thickness.

	Alcoholic solution of shellac, the proportion being that of spirit varnish	25% shellac in U. S. P. Ammonia	25% shellac in 10% ammonia water	25% shellac in equal portions of alcohol and NH_3
Rate of solubility in gastric fluid to complete disintegration	1½ to 2 hrs.	3 to 4 hours	4 to 5 hours	10 hours
Rate of solubility in intestinal fluid to complete disintegration	½ hour	5 to 10 minutes	5 to 15 minutes	10 to 15 minutes

	Alcoholic solution of shellac, the proportion being that of spirit varnish	25% shellac in U. S. P. Ammonia	25% shellac in 10% ammonia water	25% shellac in equal portions of alcohol and NH_3
Sol. in distilled water	Softens and scales off	Swells and scales off	Swells but not nearly as marked as ←	Slight swelling Coat breaks off entirely
Physical appearance of coat	Hard, shiny Not easily broken	Hard but shows tendency to crack several hrs. after coating	Coat harder and not as easily broken as ←	Hard, shiny and not easily broken
Mechanical details in coating	Cold blast of air—no marked penetration of solvent	Warm blast marked penetration and softening of tablet	Warm blast slight penetration into tablet	Warm blast no marked penetration Tackiness of coating sol. reduced

Test tablets for determining the effectiveness of the coatings showing good results in vitro were prepared to be taken internally. Each tablet contains:

Methylene blue	¼ gr.
Calcium sulphide	½ gr.
Dextrin	1 gr.
Starch	1 gr.
Sugar	2¼ gr.

Water q. s. to granulate.

These so-called "double check" tablets may be used advantageously for such purpose. If the tablet in the course of digestion loses its coating in the stomach, the acid contents will react with calcium sulphide, giving rise to eructations of hydrogen sulphide gas. If, however, the tablet passes through the stomach and then loses its coat in the intestinal fluid, a blue coloration in the urine will be observed. Should neither of these reactions be noticed, it is ample evidence to show that the tablet has passed through the entire digestive tract untouched.

The test tablets were coated with the 25 per cent. shellac in equal parts of alcohol-ammonia solution and a number of such distributed for internal administration. In nearly all cases no eructation of gas was reported but marked coloration of the urine resulted.

III.

Solubilities of Representative Manufactured Enteric Tablets

	Stomach Digestion	*Intestinal Digestion*
1. Pancreatin	*2-2½ hours	15-20 minutes
2. Glandular	1½-2 hours	15 minutes
3. Pancreatin	1½-2 hours	15-25 minutes
4. Pancreatin	2-2½ hours	25-35 minutes
5. Glandular (Keratin coating)	1-1½ hours	30 minutes
6. Pancreatin capsule (glutoid coating) special	1½ hours (swells)	1½ hours
7. Acriflavine	2 hours	1-1½ hours
8. Special glutoid	1½ hours (swells)	1½ hours

*The time referred to is that required for complete disintegration.

Summary

1. Ammoniacal solutions of shellac prove to be far more effective as enteric coatings than any of the others investigated in this work. Evidently ammonia reacts with the aliphatic acids in shellac changing its character.

2. From a mechanical standpoint it is easier to control the coating operation in the pan with such solutions because the tackiness of the shellac is reduced.

3. Of the manufactured enteric tablets none are satisfactory from every angle.

4. The spraying of volatile coating solutions should be developed with the proper equipment but cannot be done in the pan.

NOTE: Further work is now under way involving the application of the x-Ray to further confirm the effectiveness of this new method of enteric coating. This will be reported upon at a later date.

BIBLIOGRAPHY

1. *A. Ph. A.*, 33; 1885, 360—Unna.
2. *J. A. Ph. A.*, 4; 1915, 947—Peacock.
3. *Proc. P. P. A.*, 38; 1915, 262—Toplis.
4. *J. A. Ph. A.*, 4; 1915, 1241—Scoville.
5. *Am. Jour. Pharm.*, Nov., 1915, ,Vol. 87, p. 518.
6. *Jour. A. Ph. A.*, Vol. X, No. 5, p. 372.
7. Merck Report, April, 1916, pp. 78-79.
8. Tschirch, "Die Harze"—Second Edition, 1906, pp. 811-830.
9. *Remington's Practice of Pharmacy*—Chapter CV.

CERTIFIED FOOD COLORS: THEIR CHARACTERISTICS AND TESTS

By M. C. Gallagher and S. E. Owen

THE MEANS AT HAND for coloring food products may be conveniently classified as vegetable,[1] animal and chemical,[2] or synthetic or the so-called coal tar dyes. Representatives of each class have at some time or other been used in the coloring of foods and drugs. To the first class belong the anthocyans, carotinoids and chlorophylls; to the second, cochineal, and to the latter, the organic dyestuffs which have been certified by the United States Department of Agriculture as safe for use in articles intended for human consumption.

Practically all the synthetic dyes are treated with sulphuric or nitric acid in their process of manufacture and these acids in turn may have been contaminated with lead, copper or arsenic in their preparation. Harmful and toxic complexes and unused dye intermediates such as are found in most industrial dyes are also apt to be present.

Laws of the various European countries and the American States have from time to time prohibited the use of certain dyestuffs in each class, and in some cases certain classes have been prohibited. Their use had been restricted by the American food inspection divisions to such an extent that at the time of the passage of the Federal Food and Drug Act, in 1906, only seven coal tar dyes were permitted. This was a very small number compared to the number actually in existence. Green's list [2] which was published in 1903 and makes no claim to completeness, contains 688, and Mulliken's published three years later describes 1475 dyes found on the American market.[4] Many times that number probably exist today, although since the passage of the Food and Drug Act only eight more have been added to the original certified list.

The procedure necessary to have a new dye certified generally requires a period of about two years. Neither the dye itself or its process of manufacture may be protected by any unexpired patents. The complete process of manufacture must have been described in some recognized publication. Names chosen for the dye must not be misleading or in any way tend to advertise any particular manufacturer. A sample of the dye is prepared in as pure form as possible and a representative sample analyzed by the method described

by the Department of Agriculture. If the analysis shows that the dye conforms with the specifications for purity, an affidavit to that effect, both from the examining chemist and the manufacturer and a detailed report from one or more reputable pharmacologists and toxicologists, is sent with a five-pound sample of the dye to the Department of Agriculture. After the dye has been examined and found harmless and suitable it is certified, provided that there is a sufficient reason for a dye of that nature which cannot be met by any others on the list.

The following dyes have been certified:[1]

Red shades:

80	(56)	Ponceau 3R.
184	(107)	Amaranth.
773	(517)	Erythrosine.
		Ponceau SX.

Orange shades:

150	(85)	Orange I.

Yellow shades:

10	(4)	Naphthol yellow S.
640	(94)	Tartrazine.
22		Yellow AB.
61		Yellow OB.
		Sunset yellow.

Green shades:

666	(433)	Guinea green B.
670	(435)	Light green SF yellowish.
		Fast green FCF.

Blue shades:

1180	(692)	Indigotine.
		Brilliant blue.

The first number in each line is that listed in the Colour Index 1924, published by the Society of Dyers and Colourists of England.[2] The number in parenthesis is the identifying number given in Green's Systematic Survey of Organic Coloring Matters, 1904 edition.[3]

Most of these are diphenylmethane or azo-compounds and owe their acidic properties to either the COOH or HSO_3 grouping. They

may be characterized by color reactions with acids and alkalies,[4] zinc dust reduction,[7] air oxidation,[8] and spectroscopic examination.[9]

Ponceau 3R [2] is a sodium salt of ethyl-dimethyl-benzene-azo-B-naphthol-disulphonic acid. It is prepared by combining amido-ethyl-dimethylbenzene with B-naphthol. It is a bright red powder, which gives a cherry red solution in water, and is not altered by solutions of strong acids, but gives a yellow precipitate on the addition of potassium hydroxide.

Amaranth [2] is a mono-azo dye made by the diazotization of naphthic acid and coupling the product with B-naphthol, 3, 6 disulphonic acid. It is a reddish brown powder which gives a magenta red solution in water. It is unchanged by hydrochloric acid but gives a more intense red on the addition of potassium hydroxide solution. With sulphuric acid it forms a violet solution which changes to bluish violet and then to magenta red on dilution with water.

Erythrosine [2] is a xanthene dye, either the sodium or potassium salt of tetra-iodo-fluorescein, made by the iodation of fluorescein in aqueous or alcoholic solution. It is a brown powder, which dissolves in water to give a cherry red solution, but shows no fluorescence in ordinary light. When hydrochloric acid is added to a solution of the dye a yellowish brown precipitate of the free color is produced. A reddish brown solution is formed with sulphuric acid which evolves iodine on heating and gives a brownish yellow precipitate on dilution with water. Potassium hydroxide forms a reddish precipitate soluble in an excess of the reagent.

Ponceau SX [5] is a sodium salt of sulpho-benzene-B-naphthol-disulphonic acid. It is prepared by combining amido-azo-benzene-disulphonic acid with B-naphthol-disulphonic acid R-. It is a brown powder which dissolves in water forming a magenta red solution. It shows no change with hydrochloric acid. A violet precipitate is obtained upon the addition of potassium hydroxide. In concentrated sulphuric acid it gives a blue solution which turns orange to red on dilution with water.

Orange I [2] is a sodium salt of p-sulpho-benzene-azo-a-naphthol, prepared by combining sulphanic acid with a-naphthol. It is a reddish brown powder which dissolves in water forming an orange solution. The addition of hydrochloric acid to an aqueous solution produces a brown precipitate. The addition of concentrated sulphuric acid to an aqueous solution gives a violet red solution, from which the dye is precipitated in a reddish brown mass on dilution with water. The

addition of potassium hydroxide to an aqueous solution changes the color to a cherry red.

Naphthol yellow S [2] is a nitro dye, the sodium or potassium salt of dinitro-a-naphthol-b-sulphonic acid may be prepared by (a) the action of nitric acid upon a-naphthol-trisulphonic acid or (b) the action of nitric acid upon a-naphthol-disulphonic acid, 1, 2, 7 or upon the nitroso compound of the latter. It is a yellow or orange yellow powder which burns with yellow scintillations. The dye is readily soluble in water, producing a yellow solution, the color of which is unaltered by either hydrochloric acid or sodium hydroxide. Potassium hydroxide, however, produces a yellow flocculent precipitate. It dissolves in concentrated sulphuric acid to give a yellow solution, which becomes brighter upon the addition of water.

Tartrazine [2] is a yellow dye, which may be classed as an azo, or more definitely as a pyrazalone dye. It is a yellow orange powder, soluble in water. The aqueous solution is unaltered by the addition of hydrochloric acid and becomes darker on the addition of sodium hydroxide. The dye dissolves in concentrated sulphuric acid to form an orange yellow solution which becomes yellow when diluted with water.

Yellow AB is an oil soluble dye made by coupling diazotized aniline with b-naphtholamine. It is an orange powder which is insoluble in water and soluble in alcohol. The resulting orange red solution is reddened by the addition of hydrochloric acid and is not altered by the addition of sodium hydroxide. With concentrated sulphuric acid the dye gives a bluish violet solution which turns red and produces an orange red precipitate on dilution with water.

Yellow OB [2] is an oil soluble, monoazo dye, made by coupling diazotized ortho-toluidine with b-naphthalamine. It is an orange powder, insoluble in water, and dissolves in alcohol to produce an orange yellow solution. The color of the alcoholic solution is reddened by the addition of hydrochloric acid and unaltered by the addition of sodium hydroxide. It dissolves in concentrated sulphuric acid to form a reddish violet solution which turns red and produces an orange red precipitate when diluted with water.

Sunset yellow FCF [5] was first certified as buttercup yellow but the name was changed so that it would not be misconstrued as being other than a coal tar dye. It is a monoazo compound, the disodium salt of the product obtained by coupling diazotized sulphanilic acid with b-naphthol-6-monosulphonic acid. It is an orange dye soluble

in water and 50 per cent. alcohol, slightly soluble in 95 per cent. alcohol. The neutral solution is a yellowish orange, which changes to a brownish red upon the addition of an alkali. No change is produced by the addition of an acid. The powder dissolves in a concentrated solution of sulphuric acid with an orange color, which changes to yellow on dilution with water.

Guinea green B [2] is a triphenylmethane dye made by the condensation of benzyl-ethyl-anilinesulphonic acid with benzaldehyde, followed by the oxidation of the subsequent compound and conversion into the mono-sodium salt. It is a dull dark green powder or bright crystalline solid, which dissolves in water to form a green solution. It turns a brownish yellow on the addition of hydrochloric acid and a blackish green on the addition of sodium hydroxide. Owing probably to the formation of the disodium salt, the aqueous solution is decolorized by the addition of an excess of sodium hydroxide. It is decolorized by the addition of a hot solution of alkalies or alkali carbonates. With concentrated sulphuric acid it forms a yellow solution which with water first turns a yellowish red and then green.

Light green CF yellowish [2] is a triphenylmethane dye, which differs from Guinea green B in that it contains one sulphonic acid group. It is a reddish brown powder which gives a green solution in water. On the addition of hydrochloric acid it gives a yellowish brown solution which gradually fades. Upon the addition of sodium hydroxide the solution is completely decolorized. With concentrated sulphuric acid it forms a yellow solution which when diluted with water turns green.

Fast green FCF [5] is also a triphenylmethane dye which differs from guinea green B in that p-hydroxy-sulpho-benzaldehyde is substituted for benzaldehyde. It exists as reddish brown or violet crystals, lumps or powder. It dissolves easily in water to form a bluish green solution. Upon the addition of a trace of hydrochloric acid the solution turns brownish orange to green. It shows the same reaction on the addition of sulphuric acid. When a trace of alkali is added the solution becomes blue, and when an excess is added it turns to a bluish violet.

Indigotine [2] or sodium indigodisulphonate is made by sulphonating indigo. It is a bluish brown or reddish brown powder which yields a blue solution in water. On adding hydrochloric acid the aqueous solution becomes a bluish violet. Further dilution with water restores the color, however. On the addition of sodium hydroxide

the aqueous solution turns a yellowish green. With concentrated sulphuric acid it forms a bluish violet solution which turns blue when diluted with water. The color of an aqueous solution of this dye fades upon exposure to light.

Brilliant blue FCF [5] is a triphenylmethane dye which was known chemically for many years although it was only recently recognized as a food color. It is the disodium salt of the product obtained by condensing benzaldehyde-ortho-sulphonic acid with ethyl-benzyl-aniline-sulphonic acid, also a triphenylmethane dye. It is a dark purple-bronze powder, which dissolves easily in water to form a blue solution. The addition of hydrochloric acid to the aqueous solution produces a green solution which changes to yellow on the addition of more acid. Alkali does not change the color of the cold solution but upon boiling it changes to violet. The dye dissolves in concentrated sulphuric acid giving a yellow color which changes to green when diluted with water. The dye is also soluble in 95 per cent. alcohol.

No limitation is put on the amount of dye that may be used in food and ordinarily the quantities used are very small, since very dilute solutions give intense colors to a large amount of material. For example, a half ounce of one of the certified dyes will color over a thousand pounds of confectionery. Therefore only a small amount of a dye is taken into the system at one time. The usual stock solution used is about 3 to 6 per cent.

For practical purposes the identification of a solution of a single dye is fairly simple. If more than one dye has been used, solvents must be used to separate them, and the procedure becomes more involved. For general work the easiest method is to (a) extract the dye, (b) separate the mixture, (c) and make tests for identification.

Many suitable solvents may be used for the extraction [11] but for laboratory procedure the method of dyeing white wool has the advantage of being very simple. Acid dyes are removed best from a slightly acid solution [12] and basic dyes are removed best from a neutral or slightly alkaline solution. Basic dyes should be removed first. The food, drug or other substance is therefore made slightly alkaline with a small amount of a 5 per cent. ammonia water. A quantity of woolen yarn is boiled in a very weak solution of sodium hydroxide, and washed very thoroughly with water to remove any natural grease. The yarn is then placed in a solution of the dye and boiled until it extracts no more color. It is then placed in a 4 per cent. solution of hydrochloric acid and again boiled. This gives a solution of the basic

dyes. By evaporating the mixture the dye is obtained in a solid form and tested for a mixture by dusting on a moistened filter paper. A small lens is also useful to detect specks of the dye or dye spots. The original food solution containing the acid dyes in solution is then acidified and boiled with more white wool until no more color is absorbed. To obtain the acid dyes free from the wool it is boiled in a 6 per cent. solution of ammonia. The solution is evaporated and the dyes which are obtained in the solid form may be tested as indicated above for the basic dyes.

Tolman,[13] Loomis,[14] Robin,[15] and Martin Claude [16] give tests to differentiate between the vegetable colors. They remain on the first wool as a dull stain, usually green. Some of the lichens turn blue, violet or purple with ammonia. However, the brilliant colors of the coal tar dyes are readily distinguished from the dull vegetable colors.[17] If desired, the tests may be run on the wool by applying a mordant, such as sodium bisulphate. The results of the tests are taken when the samples are wet, as they sometimes fade or return to their original shade on drying.

There are a few general statements which may be made regarding the chemical properties of the dyes which may be helpful to the analyst. (a) Basic dyes are precipitated from their aqueous solution by tannin, while acid dyes are not. (b) Basic dyes generally dissolve in amyl alcohol to give a colorless or faintly colored solution. By evaporating and applying acetic acid the color is intensified. Acid dyes impart no color to amyl alcohol. (c) Basic dyes are generally dissolved by ether while acid dyes are generally left in the water solution. (d) If calcined magnesia and a small amount of a 25 per cent. solution of mercuric acetate are added to a solution suspected to contain a coal tar dye, and the whole boiled and filtered, coal tar dyes are indicated by a colored filtrate or a color in the filtrate on the addition of acetic acid. (Robin's test.)

Tests Made on White Wool and Colors as Noted When Wet

Dye	water	dil. sulph. acid	con. sulph. acid	con. HCl	dil. HCl	10% NaOH	ammonium hydroxide
Erythrosine	red	brown-yellow	orange-yellow	orange-yellow	orange	no change	no change
Amaranth	red	violet	violet-brown	dark violet	dark violet	dull brown	no change
Ponceau 3R	red	red	little change	little change	little change	dull orange	little change
Ponceau SX	red	orange-red	blue	no change	no change	violet	violet
Fast green FCF	green	yellow	pale brown	yellow	yellow	no color	no color
Guinea green B	green	orange-yellow	brown-yellow	yellow	orange-yellow	no color	no color
Light green SF Yellowish	green	yellow	orange	yellow	yellow	no color	no color
Indigotine	blue	violet-blue	darker blue	darker blue	blue	green-blue	green-blue
Brilliant blue FCF	blue	green	yellow	yellow	green	no change	no change
Orange I	orange	violet	violet	violet	violet	dark-dull red	dark-dull red
Naphthol yellow S	yellow	pale yellow	dull brown	nearly decolorized	nearly decolorized	no change	no change
Tartrazine	yellow	yellow	dark yellow	dark yellow	no change	no change	no change
Sunset yellow FCF	reddish-yellow	orange-yellow	orange	red	light red	dark red	brown-red
Yellow OB	Oil soluble						
Yellow AB	Oil soluble						

The concentration of the dye solutions used was 2 per cent. Yellow OB and Yellow AB are oil soluble and therefore it is very difficult to test them by the dyeing method.

The strength of reagents used was as follows: (a) dilute sulphuric acid, 10 per cent., (b) concentrated hydrochloric acid 30 per cent., (c) concentrated sulphuric acid 40 per cent., (d) sodium hydroxide solution 10 per cent., (e) ammonium hydroxide solution 25 per cent., (f) dilute hydrochloric acid 10 per cent.

Summary

A review of the history of the use of food colors and the laws governing them is given.

A list of the dyes approved by the United States Department of Agriculture with their chemical composition, physical properties and color reactions with both acids and alkalies, is given.

A scheme for dye separation and analysis is proposed.

BIBLIOGRAPHY

1. *Bull. U. S. Dept. Agri. Food, Drug and Insect Div.,* Ser. and Reg. Sup. No. 1. "Certification of Coal Tar Food Colors," April (1929).

2. "Colour Index Society of Dyers and Colourists," England (1924).

3. "Systematic Survey of Organic Coloring Matters," Green (1904).

4. "Identification of Pure Organic Compounds," Mulliken, N. York, Vol. VI (1917).

5. *U. S. Dept. Agri. Food, Drug and Insect Div.,* Ser. and Reg. Supplementary Letter to Certifiers, March 30, 1929.

6. *U. S. Dept. Agri. Food, Drug and Insect Div.,* Ser. and Reg. Supplementary Letter to Certifiers, July 15, 1929.

7. *J. Soc. Dyers and Colourists,* 9, 236 (1905).

8. *J. Soc. Chem. Ind.,* 12, 3 (1893).

9. *Zeit Chem. Anal.,* 26, 100 (1887).

10. National Aniline and Chemical Co., Inc., "Source of Pure Certified Samples of the Dyes."

11. *Jour. Am. Assoc. Off. Agric. Chem.,* 1, 116 and 472 (1917).

12. *Jour. Am. Chem. Soc.,* 22, 582 (1900).

13. *Jour. Am. Chem. Soc.,* 27, 213 (1905).

14. *U. S. Dept. Agric. Bur. Chem. Circ.,* 63, 47-48.

15. Girard et Dupre, *Analyse des Materies Alimentires,* Paris, pp. 678-679 (1894).

16. *Jour. Ph. Chim.,* 13, 174 (1901).

17. *Jour. Am. Assoc. Off. Agric. Chem.,* IV, 172 (1920).

Pharmacognosy Laboratory
University of Illinois
School of Pharmacy
March 17, 1930.

MEDICAL AND PHARMACEUTICAL NOTES

PHARMACEUTICAL RESEARCH—The need for funds to carry on researches in the field of pharmacy was forcefully brought to the attention of the public in a recent report submitted to the American Association of Colleges of Pharmacy by its retiring president, Professor J. G. Beard, of the University of North Carolina.

"Some months ago," said Professor Beard, "announcement was made that the late Stuart Wyeth, ex-president of John Wyeth and Son, Philadelphia, had willed unconditionally the sum of $5,000,000 to Harvard University. Such bequests are not unusual but, unfortunately, they are nearly always made either to universities like Harvard, Princeton or Chicago, that have no departments of pharmacy, or else for specific non-pharmaceutical purposes to institutions having schools of pharmacy. The result is that only on the rarest occasion does pharmacy participate in the gifts made. It is becoming increasingly the custom for persons of great wealth to make wills specifying that a generous share of their estate is to be used for educational and scientific purposes. I cannot but feel that pharmacy fails to benefit from such philanthropies because the donors were not made aware that the science of drugs is in crying need of funds with which to expand and extend its usefulness to humanity. The average layman looks upon health preservation and disease control as falling solely within the province of physicians, and when money is willed to further these ends the gift is made to institutions of medicine. The public is ignorant of the part that pharmacy plays in such a campaign and therefore fails to realize that a tremendous power for good would be set in motion were drug research properly endowed. No disparagement to the science of healing is intended and no invidious comparison is implied when the statement is made that medical science is being hindered in its progress because the study of medicine per se is subordinated to investigations less important. Research in other fields of human betterment is richly supplied with adequate funds and facilities, but extensive research in pharmacy is limited largely to drug manufacturers who necessarily must commercialize more or less whatever results they obtain. The reason and the remedy for the paucity of real research in our field are obvious. Money! Men

are available but means are lacking. If the actual situation were properly presented to the alumni of our colleges and by them passed on to men of wealth seeking a wise way in which to endow worthy causes, I believe there would be a gradual awakening to wonderful opportunities hitherto neglected. Pharmacy and the public would, of course, profit from this form of beneficence."

MEDICINAL WATERS AND THE LAW—"An important purpose of the Federal Food and Drugs Act is to enable purchasers to buy bottled waters as well as other foods and drugs for what they really are," says J. W. Sale, in charge of the water and beverage laboratory, Food and Drug Administration, United States Department of Agriculture.

False label statements and adulteration due to pollution are the two principal violations of the act found in mineral waters shipped in interstate and import commerce.

Misbranding consists chiefly in false and misleading therapeutic claims or the undeclared addition of salts, carbon dioxide or the like. Some seizures have resulted from improper statement of the quantity of contents or incorrect statement of analysis appearing on the label.

There is no objection on the part of the Food and Drug Administration to the fortification of a water with minerals if the label clearly shows the additions, says Mr. Sale. Under the law a purchaser is entitled to know whether or not a water has been modified. The statement of quantity of contents should be accurate, plain and conspicuous, in terms of liquid measure and in terms of the largest unit contained in the bottle.

Incorrect analysis is usually due to the fact that the water is analyzed at the spring, or, in the case of highly mineralized waters, it may be due to variations in composition. Statements indicating an impossible degree of accuracy in chemical analysis, or including constituents present in infinitesimal amounts are regarded as of doubtful propriety.

"The highest degree of radioactivity of a permanent nature found in any natural bottled water examined," says Mr. Sale, "was so small that to get a minimum daily dosage one would have to drink nearly 2000 gallons. Therapeutic claims for radium content it is very evident are not justifiable. Other therapeutic claims should be limited to the benefits obtainable from drinking the water without reference to special care or treatment."

In the case of pollution, control by the administration is very rigid. The polluted water is immediately removed from the market. In shipments of small containers the Federal inspector collects five bottles; when the bottles contain five or more gallons three are taken and examined. The standards employed by the Federal Food and Drug Administration in judging the sanitary condition of bottled waters are essentially the same as those used by the United States Public Health Service and are as follows:

All water subject to the food and drugs act

(1) Should be obtained from sources free from pollution or should be subjected to suitable purification.

(2) Should be bottled or otherwise prepared for the market under sanitary conditions, with special reference to the condition of the bottles, cans, drums, tank cars, or other containers and their stoppers.

(3) Should show the presence of organisms of the B. coli group:

(a) in not more than one out of five 10 cc. portions, collected from five containers holding less than one gallon;

(b) in not more than one out of three 10 cc. portions, collected from three containers holding one to five gallons; or

(c) in not more than one out of five 10 cc. portions collected from one container holding more than five gallons.

(4) Should be of good sanitary quality when judged by the results of a bacteriological examination to determine the numbers of bacteria growing on gelatin at 20 degrees C. and on agar at 37 degrees C.

(5) Should be of good sanitary quality when judged by the results of a sanitary chemical analysis, special significance being attributed to the presence of nitrite, to free ammonia in excess of 0.05 mg. per liter, and to an undue amount of organic matter.

The methods of analysis of the American Public Health Association are employed in the bacteriological examinations and the methods of either the American Public Health Association or the Association of Official Agricultural Chemists are employed for the sanitary chemical examinations.

TANNIC ACID TREATMENT OF BURNS—The fatal results of severe burns are due, in many cases, to the absorption into the circulation of toxic substances derived from protein decomposition at the site of the injury. A condition of extreme toxemia is thereby produced usually in twelve to twenty-four hours after the injury, and characterized by a marked rise in temperature, a rapid, feeble pulse, rapid breathing, a dusky-colored skin, and often "coffee-ground" vomiting, followed by delirium and death. This condition can be prevented by the early application of tannic acid, which coagulates all damaged tissues, forming an impermeable layer preventing the absorption of toxins. The patient is put to bed, the bedclothes being supported by a cage. The site of the injury is cleansed with some antiseptic agent such as ether, if necessary under an anesthetic. Tannic acid is then applied in 2.5 per cent. solution in warm sterile water by means of an atomizer and the application dried, by a current of warm air, if possible. The application of the solution is repeated at hourly intervals, until, usually in eight to twelve hours, a thin brown leathery coagulum is formed. Since tannic acid in aqueous solution is slowly hydrolyzed to gallic acid which does not precipitate proteins, the solution should be fresly prepared for each case, but need not be made freshly for each application. Care must be taken to avoid spraying the solution into the nose and ears, and especially into the eyes, which might cause coagulation of the cornea; these parts should be protected by damp cotton wool. If the whole of the damaged area cannot be sprayed at one time, as when back and chest are affected, one part may be sprayed, while to the other part the solution is applied by means of gauze compresses. Sterile gauze swabs, very lightly wrung out of the warm solution, are applied to the burn and kept in position by means of cotton wool and a bandage. These dressings are renewed and the injury examined after eight hours, and then every four hours. To facilitate removal the swabs may be moistened with more solution. By this method coagulation is effected in twelve to twenty hours. Where possible, the coagulated area is left exposed to the air, the bedclothes being supported by a cage, and care being taken not to damage the film. Parts subjected to pressure may be protected by dry gauze and cotton wool; moist dressings must on no account be applied over a coagulum. After eight to fourteen days the surface beneath the coagulum becomes coated with epithelium, when the film readily peels off. Should any raw areas remain, they may be covered with a sterilized dressing of

some bland ointment. This treatment may be usefully employed until seventy-two hours after the injury, and is not affected by the previous application of other substances, such as picric acid, but grease must first be removed. The treatment is painless, the parts becoming insensitive after two or three applications, and the formation of scar tissue, with its tendency to contract and produce deformities, is reduced to a minimum. In cases where immediate hospital treatment is not available, a first-aid dressing may be applied consisting of lint soaked in warm tannic acid solution which has been sterilized by the addition of mercuric chloride (1 in 2000).—(W. C. Wilson, Medical Research Council, Special Report Series, No. 141, H. M. Stationery Office, through *Pharm. Jour.*)

MINERAL OIL AND CANCER—Evidence that the refined mineral oils used medically will not cause cancer has just been reported to the American Medical Association by Dr. Francis Carter Wood, of the Columbia University Institute of Cancer Research.

The fact that cancer frequently occurred in human beings as a result of contact with lubricating oils has caused considerable alarm among patients who were taking mineral oil for medical purposes. Dr. Wood's scientific experiments showed that there is no ground for this alarm.

Dr. Wood tested the effects of mineral and lubricating oils, both externally and internally, on white mice of a strain whose history and liability to develop cancer were known. Several well-known makes of medical mineral oil were used.

He painted the skin of the mice with the mineral oil of the type used medically but no cancer developed. Then he painted them with heavy lubricating oil and produced a few tumors. Painting with tar produced both tumors and cancer.

Feeding both the mice and white rats with medicinal oil did not cause cancer of the gastro-intestinal tract.

The skin of the white mouse is quite as sensitive to oil irritation as the human skin, and both white mice and rats have spontaneous cancer of the intestine. Consequently if the refined oils used did not produce cancer in these animals, there is no reason to believe that it will produce cancer in human beings, Dr. Wood concluded.

Incidentally he pointed out that petrolatum has been used extensively in recent years as the basis of medical ointments, as well as for internal medication, but no cancer has been reported as a

result. Also a lighter grade of mineral oil has been used for nasal sprays without any evidence of cancer or other inflammation resulting.

These general observations, together with the scientific experiments, seem to dispel definitely the fear of getting cancer from mineral oil of the type used for medical treatment.—(*Science Service.*)

NEW DRUGS BY THOUSANDS AWAIT DISCOVERY—Never in the history of the world have the possibilities of adding to the list of valuable drugs been so great as at the present time, Dr. Reid Hunt, president of the United States Pharmacopœial Convention, declared at the opening session of the convention's decennial meeting.

We may yet get more drugs from the plant and animal kingdoms. There is no limit to the number that the chemist and the pharmacologist may synthesize in their laboratories. But even more important is the possibility that new and important uses may be found for drugs which we already have, Dr. Hunt said. He is professor of pharmacology at Harvard Medical School.

Some of the saddest pages in the history of mankind have written on them the failure of physicians to see the possibilities for treating disease with well-known chemicals. Ether was known to doctors and chemists for nearly 300 years before it was used as an anesthetic, Dr. Hunt pointed out. Another drug, amyl nitrite, a few drops of which relieves the frightful agony of one form of heart disease, was well known to chemists for twenty-three years before it was used to treat this condition. The same delayed application was repeated in the case of other anesthetics and many other drugs. They were well known chemically for years before anyone tried them in the treatment of disease and for the relief of pain. Today, said Dr. Hunt, "relief may be obtained anywhere in the world for a few cents which fifty years ago was beyond the reach of any potentate or Crœsus."

Research is needed to investigate the medical possibilities of the 258,000 organic compounds which chemists have already carefully described chemically and physically, Dr. Hunt said. New compounds are being added to the list at the rate of about twenty a day. Dr. Hunt declared America's facilities for studying the medical applications of these new compounds are very inadequate compared with research activity in Germany and other European countries.—(*Science Service.*)

NEWS ITEMS AND PERSONAL NOTES

PHARMACY GRADUATES IN NUMEROUS ACTIVITIES—The common belief, particularly today, is that practically all the graduates of colleges of pharmacy go directly into retail drug stores and stay there the rest of their lives.

To get the actual facts on the occupations which pharmacy graduates really do follow, a special tabulation was made of fifteen classes of the Philadelphia College of Pharmacy and Science. The fifteen classes were divided into three five-year groups to get the facts about graduates of various ages. The first group included the graduates from 1891 to 1895 inclusive—men who had been out of college thirty-five to forty years. The second group included the graduates of the class from 1901 to 1905—men out of college from twenty-five to thirty years. In the third group—the classes from 1911 to 1915 inclusive—were men who have been out of college fifteen to twenty years.

The analysis of occupations of the Philadelphia College graduates from 1891 to 1895 shows them today to be engaged in twenty-six distinct lines of activity. The group from 1901 to 1905, whose present addresses and occupations are known, are in twenty-seven different occupations. And in the third group, the men who left college fifteen to twenty years ago, whose present addresses and occupations are known—the classes 1911 to 1915—are today engaged in twenty-five different occupations.

Undoubtedly this list would be swelled considerably if the addresses and employments of all graduates were available.

In all three groups of these graduates those engaged in retail pharmacy are, of course, most numerous. Practically all of them operate stores of their own. In the classes from 1891 to 1895 the next most numerous group is physicians. The other occupations and professions into which graduates have gone in the order of their importance are as follows:

Manufacturing chemists.
Public office.
Salesmen for pharmaceutical manufacturers.
Executives in manufacturing enterprises.
Teaching.
Pharmacists in hospitals and other institutions.

Other occupations in which numerous graduates of these classes have gone include banking, the wholesale drug trade, pharmaceutical journalism, the military services and farming. Two are ministers, one is a dentist, another an optometrist, one is an undertaker and three are in the wholesale grocery business. Four are in the United States Government Civil Service in professional positions.

As mentioned, the occupations of the graduates of the classes of 1901 to 1905 are equally varied although about half the class is engaged today in retail pharmacy, usually as store proprietors. The other graduates are employed in such varied activities as the management of an advertising agency, the practice of veterinary medicine, real estate brokerage, investment banking and insurance underwriting.

Second position as the most popular occupation with this group of graduates has shifted from medicine to technical positions with pharmaceutical manufacturers. Physicians, however, rank third in number, followed in order by salesmen for pharmaceutical manufacturers, public officers, institutional pharmacists, teachers and wholesale druggists.

Two graduates are full time secretaries of pharmaceutical associations and five are in the Government service. One is a dentist, two are authors, and eight are executives in pharmaceutical manufacturing houses.

In the most recent group of graduates, the graduates who left the Philadelphia College in the past fifteen to twenty years, those engaged in retailing today number again a little more than 50 per cent. of the total. Second place is occupied again by chemists and pharmacists in manufacturing establishments. This time third place goes to salesmen and detail men of pharmaceutical manufacturers, closely followed by physicians in fourth place. The other occupations in which numbers of graduates are engaged are, in order:

Institutional pharmacists.

Teaching.

Executives of pharmaceutical manufacturing houses.

The wholesale drug trade.

Just as varied as the numerous occupations in which pharmacists graduated from the Philadelphia College are engaged are the localities in which they now reside. Of the group of graduates in the classes from 1891 to 1895, twenty-nine states and four foreign countries now claim them as residents. It is natural that Pennsylvania should lead the list, followed by New Jersey, but every other section of the country

is represented by several graduates from these classes. The same thing is true of the classes from 1901 to 1905. They now reside in thirty-four different states from coast to coast and in several foreign countries.

The graduates who left the Philadelphia College in the past fifteen to twenty years also are now scattered throughout the United States. Thirty-three states claim them as residents, in addition to four foreign countries. In fact, from these three classes alone forty-four states and the District of Columbia as well as eight foreign countries claim Philadelphia College graduates as residents. Undoubtedly this total would be raised to a much higher figure if the present addresses of all graduates were known. It is natural that the graduates whose present activities are least known would be scattered furthest from their alma mater.

MELLON INSTITUTE BIBLIOGRAPHIC LIST—The third annual supplement to Bibliographic Bulletin No. 2 of Mellon Institute of Industrial Research, Pittsburgh, Pa., has just been issued. This publication lists seven bulletins, fifty research reports, fifty-nine other papers and sixteen domestic and fifteen foreign patents by members of the institute during the calendar year 1929. The total contributions to the literature for the eighteen years ended January 1, 1930, have been as follows: Fifteen books, ninety-six bulletins, 528 research reports, 849 other articles, 407 United States patents, and 295 foreign patents.

Complimentary copies of the third supplement, as well as of the preceding numbers of the series, will be sent to laboratory directors, librarians, science teachers, and institutional heads who request them.

BOOK REVIEWS

PHARMACEUTICAL MATHEMATICS, by Edward Spease, Dean of Pharmacy, Western Reserve University. McGraw-Hill Book Company, Inc., N. Y., Publishers. 126 pages 5 4/5 x 8½. $1.75.

A textbook to be used between teacher and student. It is well written with careful and complete explanations, is remarkably free from errors and contains a good index. It takes up all the arithmetical problems commonly met with in the drug store, in the manufacturing laboratory and in the hospital pharmacy.

Answers to the problems are not included in the book, but perhaps that is as it should be for use between teacher and student.

R. L. C.